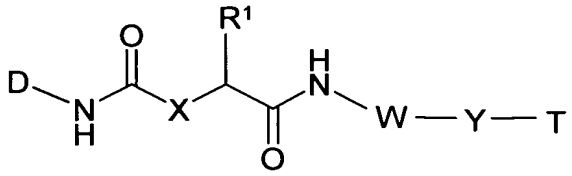
Patent Claims

1. Compounds of the formula I



I

in which

D denotes phenyl or pyridyl, each of which is unsubstituted or mono- or polysubstituted by Hal, A, OR^2, $N(R^2)_2$, NO_2, CN, $COOR^2$ or $CON(R^2)_2$,

R^1 denotes A, which is mono-, di- or trisubstituted by $S(O)_mR^2$, $SO_2N(R^2)_2$, SO_3R^2, $S(=O)(=NR^2)R^2$, $NR^2SO_2R^2$, OSO_2R^2, $OSO_2N(R^2)_2$ or $PO(OR^2)_2$ and may additionally be mono- or disubstituted by OR^3, $N(R^3)_2$, CN, $COOR^3$ or $CON(R^3)_2$,

R^2 denotes H, A, $-[C(R^3)_2]_n$-Ar', $-[C(R^3)_2]_n$-Het', $-[C(R^3)_2]_n$-cycloalkyl, $-[C(R^3)_2]_n-N(R^3)_2$ or $-[C(R^3)_2]_n-OR^3$,

R^3 denotes H or A,

W denotes $-[C(R^3)_2]_n-$,

X denotes NR^3 or O,

Y denotes alkylene, cycloalkylene, Het-diyl or Ar-diyl,

T denotes a mono- or bicyclic saturated, unsaturated or aromatic carbo- or heterocycle having 0 to 4 N, O and/or S atoms, which may be mono-, di- or trisubstituted by =O, R^2, Hal, A, $-[C(R^3)_2]_n$-Ar, $-[C(R^3)_2]_n$-Het, $-[C(R^3)_2]_n$-cycloalkyl, OR^2, $N(R^2)_2$, NO_2, CN, $COOR^2$, $CON(R^2)_2$, NR^2COA, $NR^2CON(R^2)_2$, NR^2SO_2A, COR^2, SO_2NR^2 and/or $S(O)_nA$, or $N(R^2)_2$

and, if Y = piperidine-1,4-diyl, also R^2 or cycloalkyl,

A	denotes unbranched or branched alkyl having 1-10 C atoms, in which one or two CH_2 groups may be replaced by O or S atoms and/or by -CH=CH- groups and/or also 1-7 H atoms may be replaced by F,
Ar	denotes phenyl, naphthyl or biphenyl, each of which is unsubstituted or mono-, di- or trisubstituted by Hal, A, OR^2, $N(R^2)_2$, NO_2, CN, $COOR^2$, $CON(R^2)_2$, NR^2COA, NR^2SO_2A, COR^2, $SO_2N(R^2)_2$, $-[C(R^3)_2]_n-COOR^2$, $-O-[C(R^3)_2]_o-COOR^2$, SO_3H or $S(O)_nA$,
Ar'	denotes phenyl which is unsubstituted or mono-, di- or trisubstituted by Hal, A, OR^3, $N(R^3)_2$, NO_2, CN, $COOR^3$, $CON(R^3)_2$, NR^3COA, $NR^3CON(R^3)_2$, NR^3SO_2A, COR^3, $SO_2N(R^3)_2$, $S(O)_nA$, $-[C(R^3)_2]_n-COOR^3$ or $-O-[C(R^3)_2]_o-COOR^3$,
Het	denotes a mono- or bicyclic saturated, unsaturated or aromatic heterocycle having 1 to 4 N, O and/or S atoms, which may be unsubstituted or mono-, di- or trisubstituted by carbonyl oxygen (=O), =S, $=N(R^2)_2$, Hal, A, $-[C(R^3)_2]_n-Ar$, $-[C(R^3)_2]_n-Het'$, $-[C(R^3)_2]_n-cycloalkyl$, $-[C(R^3)_2]_n-OR^2$, $-[C(R^3)_2]_n-N(R^3)_2$, NO_2, CN, $-[C(R^3)_2]_n-COOR^2$, $-[C(R^3)_2]_n-CON(R^2)_2$, $-[C(R^3)_2]_n-NR^2COA$, $NR^2CON(R^2)_2$, $-[C(R^3)_2]_n-NR^2SO_2A$, COR^2, $SO_2N(R^2)_2$ and/or $S(O)_nA$,
Het'	denotes a mono- or bicyclic saturated, unsaturated or aromatic heterocycle having 1 to 4 N, O and/or S atoms, which may be unsubstituted or mono- or disubstituted by carbonyl oxygen, =S, $=N(R^3)_2$, Hal, A, OR^3, $N(R^3)_2$, NO_2, CN, $COOR^3$, $CON(R^3)_2$, NR^3COA, $NR^3CON(R^3)_2$, NR^3SO_2A, COR^3, $SO_2N(R^3)_2$ and/or $S(O)_nA$,
Hal	denotes F, Cl, Br or I,
m	denotes 1 or 2,
n	denotes 0, 1 or 2,
o	denotes 1, 2 or 3,

and pharmaceutically usable derivatives, salts, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

2. Compounds according to Claim 1, in which

D denotes phenyl which is unsubstituted or mono- or disubstituted by Hal, A, OR^2 or $COOR^2$, or pyridyl which is unsubstituted or monosubstituted by Hal,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

3. Compounds according to Claim 1 or 2, in which

D denotes phenyl which is monosubstituted by Hal,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

4. Compounds according to one or more of Claims 1-3, in which

R^2 denotes H or alkyl having 1, 2, 3, 4, 5 or 6 C atoms,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

5. Compounds according to one or more of Claims 1-4, in which

Het denotes a mono- or bicyclic saturated, unsaturated or aromatic heterocycle having 1 to 2 N, O and/or S atoms, which may be unsubstituted or mono- or disubstituted by carbonyl oxygen, OH or OA,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

6. Compounds according to one or more of Claims 1-5, in which

Y denotes Ar-diyl,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

7. Compounds according to one or more of Claims 1-8, in which

Ar denotes phenyl which is unsubstituted or mono-, di- or trisubstituted by Hal, A, OR^2, SO_2A, SO_2NH_2, $COOR^2$ or CN,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

8. Compounds according to one or more of Claims 1-7, in which

R^1 denotes alkyl having 1, 2, 3, 4, 5 or 6 C atoms which is monosubstituted by $S(O)_mR^2$, $SO_2N(R^2)_2$, SO_3R^2, $S(=O)(=NR^2)R^2$, $NR^2SO_2R^2$, OSO_2R^2, $OSO_2N(R^2)_2$ or $PO(OR^2)_2$,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

9. Compounds according to one or more of Claims 1-8, in which

X denotes NH or O,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

10. Compounds according to one or more of Claims 1-9, in which

T denotes a mono- or bicyclic saturated, unsaturated or aromatic heterocycle having 1 to 2 N and/or O atoms, which may be mono- or disubstituted by =O, OH or OA,

or $N(R^2)_2$

and, if Y = piperidine-1,4-diyl, also R^2 or cycloalkyl,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

11. Compounds according to one or more of Claims 1-10, in which

Y denotes phenylene which is unsubstituted or monosubstituted by A,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

12. Compounds according to one or more of Claims 1-11, in which

W denotes absent,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

13. Compounds according to one or more of Claims 1-12, in which

D denotes phenyl which is monosubstituted by Hal,

R^1 denotes alkyl having 1, 2, 3, 4, 5 or 6 C atoms which is monosubstituted by $S(O)_mR^2$, $SO_2N(R^2)_2$, SO_3R^2, $S(=O)(=NR^2)R^2$, $NR^2SO_2R^2$, OSO_2R^2, $OSO_2N(R^2)_2$ or $PO(OR^2)_2$,

R^2 denotes H or alkyl having 1, 2, 3, 4, 5 or 6 C atoms,

W denotes $-(CH_2)_n-$,

X denotes NH or O,

Y denotes Ar-diyl,

T denotes a mono- or bicyclic saturated, unsaturated or aromatic heterocycle having 1 to 2 N and/or O atoms which is mono- or disubstituted by =O,
or $N(R^2)_2$
and, if Y = piperidine-1,4-diyl, also R^2 or cycloalkyl,

A denotes unbranched or branched alkyl having 1-10 C atoms, in which one or two CH_2 groups may be replaced by O or S atoms and/or by -CH=CH- groups and/or also 1-7 H atoms may be replaced by F,

Ar denotes phenyl which is unsubstituted or mono-, di- or trisubstituted by Hal, A, OR^2, SO_2A, SO_2NH_2, $COOR^2$ or CN,

Hal denotes F, Cl, Br or I,

m denotes 1 or 2,

n denotes 0, 1 or 2,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

14. Compounds according to one or more of Claims 1-13, in which

D denotes phenyl which is monosubstituted by Hal,

R^1 denotes alkyl having 1, 2, 3, 4, 5 or 6 C atoms which is monosubstituted by $S(O)_mR^2$, $SO_2N(R^2)_2$, SO_3R^2, $S(=O)(=NR^2)R^2$, $NR^2SO_2R^2$, OSO_2R^2, $OSO_2N(R^2)_2$ or $PO(OR^2)_2$,

R^2 denotes H or alkyl having 1, 2, 3, 4, 5 or 6 C atoms,

W denotes $-(CH_2)_n-$,

X denotes NH or O,

Y denotes Ar-diyl,

T denotes piperidin-1-yl, 2-oxopiperidin-1-yl, 2-oxopyrrolidin-1-yl, pyrrolidin-1-yl, 2-oxo-1*H*-pyridin-1-yl, 3-oxomorpholin-4-yl, morpholin-4-yl, 4-oxo-1*H*-pyridin-1-yl, 2,6-dioxopiperidin1-yl, 2-oxopiperazin-1-yl, 2,6-dioxopiperazin-1-yl, 2,5-dioxopyrrolidin-1-yl, 2-oxo-1,3-oxazolidin-3-yl, 3-oxo-2*H*-pyridazin-2-yl, 2-caprolactam-1-yl (= 2-oxoazepan-1-yl), 2-hydroxy-6-oxopiperazin-1-yl, 2-methoxy-6-oxopiperazin-1-yl, 2-azabicyclo[2.2.2]octan-3-on-2-yl, 5,6-dihydro-1*H*-pyrimidin-2-oxo-1-yl, 2-oxo-1,3-oxazinan-3-yl or 4*H*-1,4-oxazin-4-yl,
or $N(R^2)_2$
and, if Y = piperidine-1,4-diyl, also R^2 or cycloalkyl,

A denotes unbranched or branched alkyl having 1-10 C atoms, in which one or two CH_2 groups may be replaced

by O or S atoms and/or by -CH=CH- groups and/or also 1-7 H atoms may be replaced by F,

Ar denotes phenyl which is unsubstituted or mono-, di- or trisubstituted by Hal, A, OR^2, SO_2A, SO_2NH_2, $COOR^2$ or CN,

Hal denotes F, Cl, Br or I,

m denotes 1 or 2,

n denotes 0, 1 or 2,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

15. Compounds according to one or more of Claims 1-14, in which

D denotes phenyl which is monosubstituted by Hal,

R^1 denotes alkyl having 1, 2, 3, 4, 5 or 6 C atoms which is monosubstituted by $S(O)_mR^2$, $SO_2N(R^2)_2$, SO_3R^2, $S(=O)(=NR^2)R^2$, $NR^2SO_2R^2$, OSO_2R^2, $OSO_2N(R^2)_2$ or $PO(OR^2)_2$,

R^2 denotes H or alkyl having 1, 2, 3, 4, 5 or 6 C atoms,

W denotes $-(CH_2)_n-$,

X denotes NH or O,

Y denotes phenylene which is unsubstituted or monosubstituted by A,

T denotes piperidin-1-yl, 2-oxopiperidin-1-yl, 2-oxopyrrolidin-1-yl, pyrrolidin-1-yl, 2-oxo-1*H*-pyridin-1-yl, 3-oxomorpholin-4-yl, morpholin-4-yl, 4-oxo-1*H*-pyridin-1-yl, 2,6-dioxopiperidin1-yl, 2-oxopiperazin-1-yl, 2,6-dioxopiperazin-1-yl, 2,5-dioxopyrrolidin-1-yl, 2-oxo-1,3-oxazolidin-3-yl, 3-oxo-2*H*-pyridazin-2-yl, 2-caprolactam-1-yl (= 2-oxoazepan-1-yl), 2-hydroxy-6-oxopiperazin-1-yl, 2-methoxy-6-oxopiperazin-1-yl, 2-azabicyclo[2.2.2]octan-3-on-2-yl, 5,6-dihydro-1*H*-

pyrimidin-2-oxo-1-yl, 2-oxo-1,3-oxazinan-3-yl or 4*H*-1,4-oxazin-4-yl,
or $N(R^2)_2$
and, if Y = piperidine-1,4-diyl, also R^2 or cycloalkyl,

A denotes unbranched or branched alkyl having 1-10 C atoms, in which one or two CH_2 groups may be replaced by O or S atoms and/or by -CH=CH- groups and/or also 1-7 H atoms may be replaced by F,

Y denotes phenylene which is unsubstituted or monosubstituted by A,

Hal denotes F, Cl, Br or I,

m denotes 1 or 2,

n denotes 0, 1 or 2,

and pharmaceutically usable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

16. Compounds according to Claim 1

2-[3-(4-chlorophenyl)ureido]-*N*-[4-(2-oxo-2*H*-pyridin-1-yl)-phenyl]-4-methanesulfonylbutyramide,

2-[3-(4-chlorophenyl)ureido]-*N*-[4-(2-oxo-2*H*-pyrazin-1-yl)-phenyl]-4-methanesulfonylbutyramide,

2-[3-(4-chlorophenyl)ureido]-*N*-[4-(3-oxomorpholin-4-yl)phenyl]-4-methanesulfonylbutyramide,

(R)-2-[3-(4-chlorophenyl)ureido]-*N*-[4-(3-oxomorpholin-4-yl)-phenyl]-4-methanesulfonylbutyramide,

(R)-2-[3-(4-chlorophenyl)ureido]-*N*-[4-(2-oxo-2*H*-pyridin-1-yl)-phenyl]-3-methanesulfonylpropionamide,

(S)-2-[3-(4-chlorophenyl)ureido]-*N*-[4-(2-oxo-2*H*-pyridin-1-yl)-phenyl]-3-methanesulfonylpropionamide,

(S)-2-[*N*-(4-chlorophenyl)carbamoyloxy]-*N*-[4-(3-oxomorpholin-4-yl)phenyl]-3-methanesulfonylpropionamide,

(R)-2-[*N*-(4-chlorophenyl)carbamoyloxy]-*N*-[4-(3-oxomorpholin-4-yl)phenyl]-3-methanesulfonylpropionamide,

(R)-2-[3-(4-chlorophenyl)ureido]-*N*-[4-(2-oxo-2*H*-pyridin-1-yl)-phenyl]-4-methanesulfonylbutyramide,

(S)-2-[3-(4-chlorophenyl)ureido]-*N*-[4-(3-oxomorpholin-4-yl)-phenyl]-3-methanesulfonylpropionamide,

2-[*N*-(4-chlorophenyl)carbamoyloxy]-*N*-[4-(2-oxo-2*H*-pyridin-1-yl)phenyl]-3-methanesulfonylpropionamide,

2-[3-(4-chlorophenyl)ureido]-*N*-[4-(3-oxomorpholin-4-yl)phenyl]-3-sulfopropionamide

2-[3-(4-chlorophenyl)ureido]-*N*-[4-(2-oxo-2*H*-pyridin-1-yl)phenyl]-3-sulfopropionamide,

(S)-2-[3-(4-chlorophenyl)ureido]-*N*-[4-(3-oxomorpholin-4-yl)-phenyl]-3-(dimethoxyphosphoryl)propionamide,

2-[3-(4-chlorophenyl)ureido]-*N*-[4-(2-oxopiperidin-1-yl)phenyl]-3-(dimethoxyphosphoryl)propionamide,

2-[3-(4-chlorophenyl)ureido]-*N*-[4-(3-oxomorpholin-4-yl)phenyl]-3-phosphonopropionamide,

2-[3-(4-chlorophenyl)ureido]-*N*-[4-(3-oxomorpholin-4-yl)phenyl]-4-(methanesulfoximinyl)butyramide,

2-[3-(4-chlorophenyl)ureido]-*N*-[4-(2-oxo-2*H*-pyridin-1-yl)phenyl]-3-sulfamoylpropionamide,

2-[3-(4-chlorophenyl)ureido]-*N*-[4-(3-oxomorpholin-4-yl)phenyl]-3-methanesulfonylaminopropionamide,

2-[3-(4-chlorophenyl)ureido]-*N*-[4-(3-oxomorpholin-4-yl)phenyl]-3-sulfamoyloxypropionamide,

(R)-2-[3-(4-chlorophenyl)ureido]-*N*-[3-methyl-4-(3-oxomorpholin-4-yl)phenyl]-3-methanesulfonylpropionamide,

(R)-2-[3-(4-chlorophenyl)ureido]-*N*-[4-(2-oxo-1,3-oxazinan-3-yl)-phenyl]-3-methanesulfonylpropionamide,

(R)-2-[3-(4-chlorophenyl)ureido]-*N*-[3-methyl-4-(3-oxomorpholin-4-yl)phenyl]-4-methanesulfonylbutyramide,

(R)-2-[3-(4-chlorophenyl)ureido]-*N*-[4-(3-oxomorpholin-4-yl)-phenyl]-3-sulfamoyloxypropionamide,

(R)-2-[3-(4-chlorophenyl)ureido]-*N*-[4-(3-oxomorpholin-4-yl)-phenyl]-3-(dimethoxyphosphoryl)propionamide,

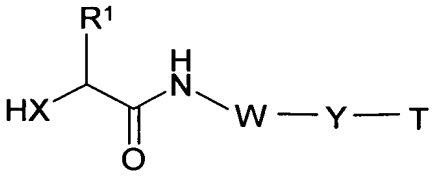
(R)-2-[3-(4-chlorophenyl)ureido]-*N*-[3-methyl-4-(3-oxomorpholin-4-yl)phenyl]-3-(dimethoxyphosphoryl)propionamide,

(S)-2-[3-(4-chlorophenyl)ureido]-*N*-[3-methyl-4-(3-oxomorpholin-4-yl)phenyl]-3-(dimethoxyphosphoryl)propionamide,

and pharmaceutically usable derivatives, salts, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

17. Process for the preparation of compounds of the formula I according to Claims 1-16 and pharmaceutically usable derivatives, solvates and stereoisomers thereof, characterised in that

a) a compound of the formula II



II

in which

R^1, T, W, X and Y have the meaning indicated in Claim 1,

is reacted with a compound of the formula III

D-N=C=O III

in which

D has the meaning indicated in Claim 1,

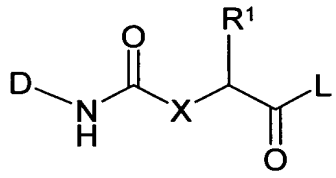
or

b) a compound of the formula IV

IV,

in which W, Y and T have the meaning indicated in Claim 1,

is reacted with a compound of the formula V



V

in which
L denotes Cl, Br, I or a free or reactively functionally modified OH group and
R^1, X and D have the meanings indicated in Claim 1,

or

c) a radical R^1 is converted into another radical R^1 by oxidising the radical R^1
and/or a base or acid of the formula I is converted into one of its salts.

18. Compounds of the formula I according to one or more of Claims 1 to 16 as inhibitors of coagulation factor Xa.

19. Compounds of the formula I according to one or more of Claims 1 to 16 as inhibitors of coagulation factor VIIa.

20. Medicaments comprising at least one compound of the formula I according to one or more of Claims 1 to 16 and/or pharmaceutically usable derivatives, salts, solvates and stereoisomers thereof, including mixtures thereof in all ratios, and optionally excipients and/or adjuvants.

21. Medicaments comprising at least one compound of the formula I according to one or more of Claims 1 to 16 and/or pharmaceutically usable derivatives, salts, solvates and stereoisomers thereof, including mixtures thereof in all ratios, and at least one further medicament active ingredient.

22. Use of compounds according to one or more of Claims 1 to 16 and/or physiologically acceptable salts and solvates thereof for the preparation of a medicament for the treatment of thromboses, myocardial infarction, arteriosclerosis, inflammation, apoplexy, angina pectoris, restenosis after angioplasty, claudicatio intermittens, migraine, tumours, tumour diseases and/or tumour metastases.

23. Set (kit) consisting of separate packs of

(a) an effective amount of a compound of the formula I according to one or more of Claims 1 to 16 and/or pharmaceutically usable derivatives, salts, solvates and stereoisomers thereof, including mixtures thereof in all ratios,

and

(b) an effective amount of a further medicament active ingredient.

24. Use of compounds of the formula I according to one or more of Claims 1 to 16 and/or pharmaceutically usable derivatives, salts, solvates and stereoisomers thereof, including mixtures thereof in all ratios,
for the preparation of a medicament for the treatment of thromboses, myocardial infarction, arteriosclerosis, inflammation, apoplexy, angina pectoris, restenosis after angioplasty, claudicatio intermittens, migraine, tumours, tumour diseases and/or tumour metastases, in combination with at least one further medicament active ingredient.